L Number	Hits	Search Text	DB	Time stamp
1	9578	plasminogen near3 (activator or activation)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:53
7	3581	streptokinase	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:54
13	7832	fibronectin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:54
19	967	fibrin near4 (bind or binding)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:55
25	119	(plasminogen near3 (activator or activation)) and streptokinase and fibronectin and (fibrin near4 (bind or binding))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:56
31	119	((plasminogen near3 (activator or activation)) and streptokinase and fibronectin and (fibrin near4 (bind or binding))) and (fusion protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:57
37	0	streptokinase near5 fibronectin and "129"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:58
43	3	streptokinase near5 fibronectin and (fibrin near4 (bind or binding))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:59
49	19	streptokinase near8 fibronectin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:59
55	2	(streptokinase near8 fibronectin) near8 (fibrin near4 (bind or binding))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/12/22 21:59

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NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
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NEWS 30	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002
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NEWS EXPRESS	October 14 CURRENT WINDOWS VERSION IS V6.01, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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=> s streptokinase (8A) fibronectin
  41 FILES SEARCHED...
  80 FILES SEARCHED...
L1          112 STREPTOKINASE (8A) FIBRONECTIN

=> s fibrin (4A) (bind or binding)
  23 FILES SEARCHED...
  53 FILES SEARCHED...
  90 FILES SEARCHED...
L2         8002 FIBRIN (4A) (BIND OR BINDING)

=> s l1 (8A) l2
  58 FILES SEARCHED...
L3           33 L1 (8A) L2

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=> s l4 (10A) streptokinase
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SEARCH ENDED BY USER

=> s l4 and streptokinase
  32 FILES SEARCHED...
  59 FILES SEARCHED...
L5   31 L4 AND STREPTOKINASE

=> d l5 1-31 bib ab

L5   ANSWER 1 OF 31 BIOTECHABS COPYRIGHT 2002 THOMSON DERWENT AND ISI
AN   2000-13074 BIOTECHABS
TI   Hybrid **streptokinase**-fibrin binding domain proteins useful for thrombolytic therapy comprises a streptokinae fused with fibrin binding domains of human fibronectin having independent fibrin binding domains of human fibronectin;
      vector-mediated gene transfer and expression in host cell
AU   Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA   CSIR-New-Delhi
LO   New Delhi, India.
PI   EP 1024192 2 Aug 2000
AI   EP 1999-310541 23 Dec 1999
PRAI IN 1998-382598 24 Dec 1998
DT   Patent
LA   English
OS   WPI: 2000-516032 [47]
AB   A hybrid plasminogen activator (PA) containing a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** having independent **fibrin binding** ability and delayed plasminogen activation. The hybrid PA possess the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration or lag after exposure of the PA to a suitable animal or human PG Also claimed are: a DNA segment encoding the hybrid PA; an expression vector; and prokaryotic or eukaryotic cells, transfrome or transfected with the vector. The hybrid **streptokinase**-fibrin binding domain proteins are useful in thrombolytic therapy for various kinds of cardiovascular disorders. (58pp)

L5   ANSWER 2 OF 31 CAPLUS COPYRIGHT 2002 ACS
AN   1992:443664 CAPLUS
DN   117:43664
TI   Polypeptides containing the fibrin-binding domain of fibronectin, their recombinant production, and their use in imaging and therapy
IN   Vogel, Tikva; Levanon, Avigdor; Werber, Moshe; Guy, Rachel; Panet, Amos; Hartman, Jacob; Shaked, Hadassa
PA   Bio-Technology General Corp., USA
SO   PCT Int. Appl., 192 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2

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	AU 660618	B2	19950706		
	JP 05508766	T2	19931209	JP 1991-511197	19910521
	HU 66189	A2	19941028	HU 1992-3516	19910521
	HU 216302	B	19990628		
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	NO 9204405	A	19930113	NO 1992-4405	19921113
	US 5455158	A	19951003	US 1993-58241	19930504
	US 5679320	A	19971021	US 1994-259569	19940614
	US 5965383	A	19991012	US 1995-409750	19950324
	US 5869616	A	19990209	US 1997-826885	19970408
	US 6121426	A	20000919	US 1997-909140	19970811
PRAI	US 1990-526397	A	19900521		
	US 1988-291951	B2	19881229		
	US 1989-345952	B2	19890428		
	CA 1989-2006929	A	19891229		
	US 1991-703842	B1	19910521		
	WO 1991-US3584	A	19910521		
	US 1993-58241	A1	19930504		
	US 1994-259569	A3	19940614		
	US 1995-409750	A3	19950324		

AB Polypeptides having amino acid sequences substantially present in the fibrin-binding domain (FBD) of human fibronectin are labeled with an imageable marker and used in imaging a thrombus or atherosclerotic plaque. Thrombolytic agents bound to the FBD polypeptides are also claimed. Wounds are treated with fusion products of the FBD polypeptide and a polypeptide comprising the cell-binding domain of human fibronectin. A human fibronectin cDNA library was prepd. and used in cloning and making various FBD polypeptides. The polypeptides were modified with DTPA and radiolabeled with 111In and shown to bind to preformed thrombi and thrombi in vivo. They gave a high thrombus:blood ratio of 80-200 after 24 h. The bacterial binding domain of fibronectin was shown to be sepd. from the FBD since a 31-kDa recombinant FBD polypeptide contg. the entire FBD (residues 1-262 of fibronectin) bound to Staphylococcus aureus, while 18.5 kDa and 12 kDa polypeptides contg. the 1st 154 and 109 amino acid residues of fibronectin, resp., did not. The 18.5 and 12 kDa polypeptides had a high covalent binding specificity for fibrin together with a narrower spectrum of activities and lower specificity for other ligands such as vascular components and bacteria than the 31 kDa protein which is advantageous for thrombus imaging.

L5 ANSWER 3 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAY90282 Protein DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223

PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents the human Streptococcus equisimilus **streptokinase** protein sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 4 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAY90281 Protein DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a human fibronectin fragment, containing fibrin binding domains. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use

of **streptokinase**.

L5 ANSWER 5 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAY90280 Peptide DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents the intergenic region of a chimeric streptkinase-fibrin binding domain (SK-FBD) protein sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 6 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37644 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident

only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 7 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37643 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 8 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37642 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223

PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 9 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37641 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence is a PCR primmer used in the construction of a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This

overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 10 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37640 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence is a PCR primmer used in the construction of a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 11 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37639 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence is a PCR primmer used in the construction of a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin

independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 12 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37638 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence is a PCR primmer used in the construction of a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 13 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37637 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M

PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 14 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37636 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without

significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 15 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37635 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 16 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37634 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA

possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 17 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37633 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents the human Streptococcus equisimilus **streptokinase** coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 18 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37632 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.

PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a human fibronectin coding sequence fragment, containing fibrin binding domains. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 19 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37631 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the human fibrin binding domain coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the

plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 20 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37630 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the human fibrin binding domain coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 21 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37629 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents the intergenic region of a chimeric streptkinase-fibrin binding domain (SK-FBD) protein coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin

independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 22 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37628 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a **streptokinase**-NTR (SK-NTR) gene (where NTR stands for N-terminally repaired with native sequence). The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 23 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37627 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M

PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 24 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37626 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a fragment of the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without

significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 25 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37625 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a fragment of the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 26 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37624 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA

possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 27 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37623 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 28 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37622 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.

PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a **streptokinase**-NTRN (SK-NTRN) gene (where NTRN stands for N-terminally repaired with native sequence). The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 29 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37621 DNA DGENE
TI Hybrid **streptokinase-fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without

significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 30 OF 31 DGENE (C) 2002 THOMSON DERWENT
AN AAA37620 DNA DGENE
TI Hybrid **streptokinase**-**fibrin binding** domain polypeptides useful for thrombolytic therapy comprises a **streptokinase** fused with **fibrin binding** domains of human **fibronectin** -
IN Sahni G; Kumar R; Roy C; Rajogopal K; Nihalani D; Sundaram V; Yadav M
PA (COUL) CSIR COUNCIL SCI IND RES.
PI EP 1024192 A2 20000802 58p
AI EP 1999-310541 19991223
PRAI IN 1998-3825 19981224
DT Patent
LA English
OS 2000-516032 [47]
AB This sequence represents a PCR primer for the Streptococcus equisimilis **streptokinase** (SK) coding sequence. The invention relates to a hybrid plasminogen activator (PA) comprises a polypeptide fusion between **streptokinase** (SK), which are capable of plasminogen (PG) activation, and fibrin binding regions of human fibronectin, which are from fibrin binding domains (FBD) 4 and 5 or 1 and 2. The hybrid PA possesses the ability to bind with fibrin independently and also characteristically retains a PG activation ability which becomes evident only after a pronounced duration, or lag, after exposure of the PA to a suitable animal or human PG. The hybrid **streptokinase**-fibrin binding domain polypeptides are useful in thrombolytic therapy for various kinds of cardiovascular disorders. The hybrids have enhanced fibrin selectivity as well as kinetics of plasminogen activation that are distinct from that of natural **streptokinase** in being characterised by a temporary delay, or lag of several minutes in the natural rate of the catalytic conversion of plasminogen to plasmin (i.e. delayed-action thrombolysis). The proteins can bind tightly with fibrin in blood clots soon after introduction into the vascular system without significantly activating the circulating blood plasminogen to plasmin, thus aiding in the localisation of the plasminogen activation process to the site of pathological thrombus. This overcomes systemic plasminogen activation encountered during clinical use of **streptokinase**.

L5 ANSWER 31 OF 31 USPATFULL
AN 92:80812 USPATFULL
TI Pharmaceutically active conjugates having improved body tissue binding specificity
IN Brown, Robert A., St. Albans, Great Britain
PA Central Blood Laboratories Authority, Borehamwood, Great Britain (non-U.S. corporation)
PI US 5151412 19920929
WO 8803810 19880602
AI US 1989-359662 19890721 (7)
WO 1987-GB854 19871127
19890721 PCT 371 date
19890721 PCT 102(e) date
PRAI GB 1986-28398 19861127
DT Utility
FS Granted
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Kim, Kay K.
LREP Foley & Lardner
CLMN Number of Claims: 18
ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1358
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutically active conjugates comprising a pharmaceutically active substance for treating a disorder of the body that involves a specified body tissue conjugated directly or indirectly with at least one fragment of an adhesive glycoprotein such as fibronectin, the said glycoprotein fragment(s) having improved binding specificity compared with the parent protein for the said body tissue.